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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,520	07/11/2001	Avi Ashkenazi	10466/83	1093

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Arnold & Porter LLP (24126)
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Washington, DC 20004-1206

EXAMINER	
LI, RUIXIANG	
ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
03/22/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/903,520	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-46 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-46, and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicant's amendments filed on 12/11/2009 and 05/14/2009 have been entered. Claims 44-46 and 49-51 are pending and under consideration.

Withdrawn Objections and/or Rejections

The rejection of claims 44, 47, 50, and 51 under 35 U.S.C. 112, 1st paragraph for written description is withdrawn in view of amended claims.

Claim Rejections under 35 USC § 112, 1st paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 44-46 and 49-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. The basis for the rejection is set forth in the previous office actions.

(iii). Response to Applicants' argument

Beginning at page 5 of Applicants' response, Applicants argue that based upon disclosure in the application coupled with information known in the art, one skilled in the art would know that agonistic immunostimulating polypeptides or antibodies are useful in treating, for instance, neoplastic tumors, or antagonistic antibodies-immunosuppressors, are useful for instance, in treating diseases like autoimmune or graft vs host disease. Applicants argue that the instant invention is directed to a product, not a method of treatment, and the product is not required to have a specifically designated use such as for treating a particular disease. .

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. The specification does not disclose any particular diseases that can be treated by the polypeptide or an antibody that binds to the polypeptide. The specification fails to provide any working examples or sufficient guidance with respect to treating a particular disease. The prior art does not provide teachings that any molecules that are tested positive in a MLR assay can be used to treat any diseases, such as tumors or autoimmune disease. The prior art teaches that no in vitro assay predicts or correlates with in vivo immunosuppressive efficacy (See, Kahan Cur. Opin. Immunol. 4:5553-560, 1992). It is unpredictable whether a molecule tested positive in a MLR assay can be used to treat a particular disease. It would require undue experimentation to use the claimed invention. Moreover, 35 U.S.C. 112, first paragraph requires the disclosure to enable the claimed invention; it does not matter whether the claimed invention is a product or a method of treatment.

Beginning at the page 7 of Applicants' response, Applicants argue that a positive result as a stimulator in the MLR assay is also characteristics of molecules which have known in vivo utilities in the treatment of disorders for which stimulation of an immune response is desirable. Applicants argue that the MLR is a widely used on vitro assay for identifying immunostimulatory compounds and that the positive result as a stimulator in the MLR assay is widely accepted as a valid indication of the therapeutic use in the treatment of diseased conditions, including irradiation of tumors.

Applicants' argument has been fully considered, but is not deemed to be persuasive because there is no evidence on the record, either disclosed in the specification or taught in the prior art, showing that a mere positive result as a stimulator in the MLR assay is a clear indicator that the molecule tested can be used to treat a particular disease, such as tumor.

On page 9 of Applicants' response, with respect to the Gubler reference, Applicants argue that the MLR assay is very useful in identifying immunostimulants. This is not persuasive because the Gubler reference does not establish that a single MLR assay, as instantly disclosed, is sufficient to identify a therapeutic agent for a particular disease.

On page 10 of Applicants' response, Applicants argue that the Peterson reference further supports the use of IL-12 in the treatment of cancer, melanoma. Applicants

argue that Peterson et al is a supportive ad enabling reference, indicating the use of immunostimulant molecule in the successful treatment of cancer. Applicants' argument has been fully considered, but is not deemed to be persuasive because the immunostimulant molecule IL-12 does not establish that each and every molecule tested positive in a MLR assay can be used to treat cancer.

From page 10 to page 13 of Applicants' response, Applicants criticize the examiner's opinions with respect to a number of cited references. Applicants argument is not persuasive because the cited references, either alone or in combination, provide a showing a mere positive result as a stimulator in the MLR assay is a clear indicator that the molecule tested can be used to treat a particular disease, such as tumor.

On page 13 of applicants' response, Applicants argue that the specification clearly indicates the claimed polypeptides are useful in the treatment of undesirable immune response. Applicants argue that the use of immunosuppressive molecules in the treatment of such disorders is well known in the art. Applicants argue that any further experimentation required for determining a particular dosage or a method for the administration of PRO335 would not be considered undue. This is not persuasive for the reasons set forth above on page 3.

Beginning at the bottom of page 13, Applicants cite MPEP and argue that there is a reasonable correlation between the disclosed in vitro utility and an in vivo activity and a

rigorous correlation is not required. Applicants argue that MLR was routinely used in the art to identify immunostimulants or immunosuppressors in the treatment of various disease and conditions. Applicants argue that one skilled in the art would know that immunostimulating compounds like IL-12 or PRO335 of this invention could be useful in immunoadjuvant therapies, for the treatment of tumors (cancer) and could be administered either alone or together with other agents to stimulate T cell proliferation/activation (immune function). Applicants argue that these could be done without undue experimentation.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the reasons above. In addition, MPEP states that "if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate". In the instant case, there is no evidence, either disclosed in the specification or taught in the prior art, showing that the in vitro MLR assay correlates to a specific condition.

For the reasons set forth above and on the record, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.
March 16, 2010